

This report is required by law (7 USC 2143) Failure to report according to the regulations can result in an order to cease and desist and to be subject to penalties as provided for in Section 2150

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UNITED STATES DEPARTMENT OF AGRICULTURE
ANIMAL AND PLANT HEALTH INSPECTION SERVICE

1. REGISTRATION NO. 31-R-0021
CUSTOMER NUMBER: 228

FORM APPROVED
OMB NO. 0579-0036

ANNUAL REPORT OF RESEARCH FACILITY
(TYPE OR PRINT)

2. HEADQUARTERS RESEARCH FACILITY (Name and Address, as registered with USDA Include Zip Code)

Battelle Memorial Institute
505 King Avenue
Columbus, OH 43201
Telephone: (614) 424-7444

3. REPORTING FACILITY (List all locations where animals were housed or used in actual research, testing, teaching, or experimentation, or held for these purposes. Attach additional sheets if necessary.)

FACILITY LOCATIONS (Sites)

See Attached Listing

REPORT OF ANIMALS USED BY OR UNDER CONTROL OF RESEARCH FACILITY (Attach additional sheets if necessary or use APHIS FORM 7023A)

A. Animals Covered By The Animal Welfare Regulations	B. Number of animals being bred, conditioned, or held for use in teaching, testing, experiments, research, or surgery but not yet used for such purposes	C. Number of animals upon which teaching, research, experiments, or tests were conducted involving no pain, distress, or use of pain- relieving drugs.	D. Number of animals upon which experiments, teaching, research, surgery, or tests were conducted involving accompanying pain or distress to the animals and for which appropriate anesthetic, analgesic, or tranquilizing drugs were used	E. Number of animals upon which teaching experiments, research, surgery, or tests were conducted involving accompanying pain or distress to the animals and for which the use of appropriate anesthetic, analgesic, or tranquilizing drugs would have adversely affected the procedures, results, or interpretation of the teaching, research, experiments, surgery, or tests. (An explanation of the procedures producing pain or distress in those animals and the reasons such drugs were not used must be attached to this report)	F. TOTAL NO OF ANIMALS (Cols. C + D + E)
4. Dogs		573	166		739
5. Cats					
6. Guinea Pigs	175	812	117	704	1,633
7. Hamsters					
8. Rabbits	8	627	52	342	1,021
9. Non-human Primates	113	583	104	92	779
10. Sheep					
11. Pigs		17	10		27
12. Other Farm Animals					
13 Other Animals					
Ferrets	31	2		18	20

ASSURANCE STATEMENTS

- 1) Professionally acceptable standards governing the care, treatment, and use of animals including appropriate use of anesthetic, analgesic, and tranquilizing drugs, prior to, during and following actual research, teaching, testing, surgery, or experimentation were followed by this research facility
- 2) Each principal investigator has considered alternatives to painful procedures.
- 3) This facility is adhering to the standards and regulations under the Act, and it has required that exceptions to the standards and regulations be specified and explained by the principal investigator and approved by the Institutional Animal Care and Use Committee (IACUC). A summary of all such exceptions is attached to this annual report. In addition to identifying the IACUC-approved exceptions, this summary includes a brief explanation of the exceptions, as well as the species and number of animals affected.
- 4) The attending veterinarian for this research facility has appropriate authority to ensure the provision of adequate veterinary care and to oversee the adequacy of other aspects of animal care and use.

CERTIFICATION BY HEADQUARTERS RESEARCH FACILITY OFFICIAL

(Chief Executive Officer or Legally Responsible Institutional Official)

I certify that the above is true, correct, and complete (7 U.S.C. Section 2143).

SIGNATURE OF HEADQUARTERS RESEARCH FACILITY OFFICIAL

(b)(6), (b)(7)(C)

DATE SIGNED

11-16-06

Summary of Exceptions to the Regulations or Standards

A. Primary Enclosures

1. Three animals were socially housed instead of pairing to provide social housing for an odd numbered group.
2. This social housing was done to promote species-typical behavior and enhance acclimation.
3. Species: Primate
4. Number of animals: 6

B. Dog Exercise

1. Exceptions were granted to the dog exercise plan.
2. These exceptions were granted for scientific reasons for an infusion study. Animals on study were not exercised during the period of data collection due to issues of catheter maintenance. The exemption was of short duration (10-14 days).
3. Species: Dog
4. Number of animals used: 32

C. Sanitization of Primary Enclosures

1. A one day delay was granted to the cage change requirement.
 - a. This delay was granted to minimize handling of neonatal animals.
 - b. Species: Rabbit
 - c. 53 (10 dams and 43 kits)
2. A one day delay was granted to the cage change requirement. The cages were cleaned twice daily as per standard procedure.
 - a. This delay was granted due to radiotelemetry data collection in close proximity.
 - b. Species: Dog
 - c. 10

Column E Explanation Form

1. Registration Number: 31-R-0021
2. Number of animals used in this study: 1
3. Species (common name) of animals used in this study: Ferret
4. Explain the procedure producing pain and/or distress: Subcutaneous injection. The dosing procedure involved an injection with a proprietary vaccine which did not cause more than momentary pain or distress. The administration of infectious material via intranasal instillation was carried out under anesthesia, and did not cause any distress, however the resultant viral infection may have caused pain and/or distress.
5. Provide scientific justification why pain and/or distress could not be relieved. State methods or means used to determine that pain and/or distress relief would interfere with test results.

Anesthetics, analgesics and sedatives may potentiate the effects of infection and could confound results. There are no known characterized, surrogate markers to predict mortality. Experienced staff veterinarians and animal technicians were on site to monitor the study conduct and any animal welfare issues. Pain-relieving drugs were not used, on the basis that death is rapid following the onset of symptoms, and that the use of pain medications could mask the clinical appearance, affecting the experimental data. Animals exhibiting clinical signs or those which were moribund were euthanized to alleviate pain and distress. These data are critical to human safety in the event of human exposure.

6. What, if any, federal regulations require this procedure? Cite the agency, the Code of Federal Regulations (CFR) title number and the specific section number:

This work was conducted to determine the efficacy of a proprietary vaccine and provide proof of concept for the development of an anti-viral prophylactic [required by the federal government under 21CFR.314.610 - subpart I -approval of new drugs when human efficacy studies are not ethical or feasible, and/or 21CFR601.91 - subpart H -approval of biological products when human efficacy studies are not ethical or feasible].

Column E Explanation Form

1. Registration Number: 31-R-0021
2. Number of animals used in this study: 17
3. Species (common name) of animals used in this study: Ferret
4. Explain the procedure producing pain and/or distress: The administration of infectious material via intranasal instillation was carried out under anesthesia, and did not cause any distress, however the resultant viral infection may have caused pain and/or distress.
5. Provide scientific justification why pain and/or distress could not be relieved. State methods or means used to determine that pain and/or distress relief would interfere with test results.

Anesthetics, analgesics and sedatives may potentiate the effects of infection and could confound results. There are no known characterized, surrogate markers to predict mortality. Experienced staff veterinarians and animal technicians were on site to monitor the study conduct and any animal welfare issues. Pain-relieving drugs were not used, on the basis that death is rapid following the onset of symptoms, and that the use of pain medications could mask the clinical appearance, affecting the experimental data. Animals exhibiting clinical signs or those which were moribund were euthanized to alleviate pain and distress. These data are critical to human safety in the event of human exposure.

6. What, if any, federal regulations require this procedure? Cite the agency, the Code of Federal Regulations (CFR) title number and the specific section number:

This work was conducted to validate a model and develop data necessary for definitive studies [required by the federal government under 21CFR.314.610 - subpart I -approval of new drugs when human efficacy studies are not ethical or feasible, and/or 21CFR601.91 - subpart H -approval of biological products when human efficacy studies are not ethical or feasible].

Column E Explanation Form

1. Registration Number: 31-R-0021
2. Number of animals used in this study: 394
3. Species (common name) of animals used in this study: Guinea Pig
4. Explain the procedure producing pain and/or distress: Intradermal injection. The dosing procedure involved an injection with bacterial spores which did not cause more than momentary pain or distress. The resultant bacterial infection may have caused pain and/or distress.
5. Provide scientific justification why pain and/or distress could not be relieved. State methods or means used to determine that pain and/or distress relief would interfere with test results.

Anesthetics, analgesics and sedatives may potentiate the effects of infection and could confound results. There are no known characterized, surrogate markers to predict mortality. Experienced staff veterinarians and animal technicians were on site to monitor the study conduct and any animal welfare issues. Pain-relieving drugs were not used, on the basis that death is rapid following the onset of symptoms, and that the use of pain medications could mask the clinical appearance, affecting the experimental data. Animals exhibiting clinical signs or those which were moribund were euthanized to alleviate pain and distress. These data are critical to human safety in the event of human exposure.

6. What, if any, federal regulations require this procedure? Cite the agency, the Code of Federal Regulations (CFR) title number and the specific section number:

This work was conducted to validate a model and develop data necessary for definitive studies [required by the federal government under 21CFR.314.610 - subpart I -approval of new drugs when human efficacy studies are not ethical or feasible, and/or 21CFR601.91 - subpart H -approval of biological products when human efficacy studies are not ethical or feasible].

Column E Explanation Form

1. Registration Number: 31-R-0021
2. Number of animals used in this study: 124
3. Species (common name) of animals used in this study: Guinea Pig
4. Explain the procedure producing pain and/or distress: Intradermal injection. The dosing procedure involved an injection with bacterial spores which did not cause more than momentary pain or distress. The resultant bacterial infection may have caused pain and/or distress. This work was conducted to evaluate the effectiveness of monoclonal antibodies, antibiotic treatment and/or vaccination (proprietary).
5. Provide scientific justification why pain and/or distress could not be relieved. State methods or means used to determine that pain and/or distress relief would interfere with test results.

Anesthetics, analgesics and sedatives may potentiate the effects of infection and could confound results. There are no known characterized, surrogate markers to predict mortality. Experienced staff veterinarians and animal technicians were on site to monitor the study conduct and any animal welfare issues. Pain-relieving drugs were not used, on the basis that death is rapid following the onset of symptoms, and that the use of pain medications could mask the clinical appearance, affecting the experimental data. Animals exhibiting clinical signs or those which were moribund were euthanized to alleviate pain and distress. These data are critical to human safety in the event of human exposure.

6. What, if any, federal regulations require this procedure? Cite the agency, the Code of Federal Regulations (CFR) title number and the specific section number:

This work was conducted to validate a model and develop data necessary for definitive studies [required by the federal government under 21CFR.314.610 - subpart I -approval of new drugs when human efficacy studies are not ethical or feasible, and/or 21CFR601.91 - subpart H -approval of biological products when human efficacy studies are not ethical or feasible].

Column E Explanation Form

1. Registration Number: 31-R-0021
2. Number of animals used in this study: 15
3. Species (common name) of animals used in this study: Guinea Pig
4. Explain the procedure producing pain and/or distress: To estimate physiological effects in human beings, guinea pigs were exposed to aerosols, or injected subcutaneously, to determine physiological effects of an unidentified compound.
5. Provide scientific justification why pain and/or distress could not be relieved. State methods or means used to determine that pain and/or distress relief would interfere with test results.

To estimate the physiological effects in man, guinea pigs were exposed to an unidentified compound. It is necessary to use a species of animal known to respond to compounds in a manner similar to that of man. There are no known characterized, surrogate markers to predict mortality. Animals exhibiting mild clinical signs often recovered without signs of pain and those with severe signs died rapidly. Anesthetics, analgesics and tranquilizers would have interfered with the physiological effects of this compound. Experienced staff veterinarians and animal technicians were on site to monitor the study conduct and any animal welfare issues. These data are critical to human safety in the event of exposure.

6. What, if any, federal regulations require this procedure? Cite the agency, the Code of Federal Regulations (CFR) title number and the specific section number:

N/A

Column E Explanation Form

1. Registration Number: 31-R-0021
2. Number of animals used in this study: 62
3. Species (common name) of animals used in this study: Guinea Pigs
4. Explain the procedure producing pain and/or distress: Animals were given toxin orally and observed for one week. The dosing procedure involved oral gavage of a bacterial toxin solution which did not

cause more than momentary pain or distress. The resultant toxicity may have caused pain and/or distress. This work was conducted to evaluate the effects of the delivery vehicle on the toxin's potency.

5. Provide scientific justification why pain and/or distress could not be relieved. State methods or means used to determine that pain and/or distress relief would interfere with test results.

Anesthetics, analgesics and sedatives may potentiate the effects of infection and could confound results. There are no known characterized, surrogate markers to predict mortality. Experienced staff veterinarians and animal technicians were on site to monitor the study conduct and any animal welfare issues. Anesthetics were not used, on the basis that death is rapid following the onset of symptoms, and that the use could mask the clinical appearance, affecting the experimental data which included telemetry implants to monitor parameters known to be altered by the use of drugs. Animals exhibiting clinical signs or those which were moribund were euthanized to alleviate pain and distress. These data are critical to human safety in the event of human exposure.

6. What, if any, federal regulations require this procedure? Cite the agency, the Code of Federal Regulations (CFR) title number and the specific section number:

N/A

Column E Explanation Form

1. Registration Number: 31-R-0021
2. Number of animals used in this study: 109
3. Species (common name) of animals used in this study: Guinea pigs
4. Explain the procedure producing pain and/or distress: Aerosol challenge with bacterial spores. The challenge was performed using a muzzle-only exposure chamber. The challenge procedure itself is not painful but resultant bacterial infection may have caused pain and/or distress.
5. Provide scientific justification why pain and/or distress could not be relieved. State methods or means used to determine that pain and/or distress relief would interfere with test results.

Anesthetics, analgesics, and sedatives could not be provided because it had the potential to mask or potentiate the effects of infection and confound results. There are no known characterized, surrogate markers to predict mortality. Experienced staff veterinarians and animal technicians were on site to monitor the study conduct and any animal welfare issues. Pain-relieving drugs were not used, on the basis that death is rapid following the onset of symptoms, and that the use of pain medications could mask the clinical appearance, affecting the experimental data. Animals exhibiting clinical signs or those which are found to be moribund were euthanized to alleviate pain and distress. These data are critical to human safety in the event of human exposure.

6. What, if any, federal regulations require this procedure? Cite the agency, the Code of Federal Regulations (CFR) title number and the specific section number:

Agency: N/A

Column E Explanation Form

1. Registration Number: 31-R-0021
2. Number of animals used in this study: 6

3. Species (common name) of animals used in this study: New Zealand White Rabbits
4. Explain the procedure producing pain and/or distress: Aerosol challenge with bacterial spores. The challenge was performed using a muzzle-only exposure chamber. The challenge procedure itself is not painful but resultant bacterial infection may have caused pain and/or distress.
5. Provide scientific justification why pain and/or distress could not be relieved. State methods or means used to determine that pain and/or distress relief would interfere with test results.

Anesthetics, analgesics, and sedatives could not be provided because it had the potential to mask or potentiate the effects of infection and confound results. There are no known characterized, surrogate markers to predict mortality. Experienced staff veterinarians and animal technicians were on site to monitor the study conduct and any animal welfare issues. Pain-relieving drugs were not used, on the basis that death is rapid following the onset of symptoms, and that the use of pain medications could mask the clinical appearance, affecting the experimental data. Animals exhibiting clinical signs or those which are found to be moribund were euthanized to alleviate pain and distress. These data are critical to human safety in the event of human exposure.

6. What, if any, federal regulations require this procedure? Cite the agency, the Code of Federal Regulations (CFR) title number and the specific section number:

Agency: N/A

Column E Explanation Form

1. Registration Number: 31-R-0021
2. Number of animals used in this study: 18
3. Species (common name) of animals used in this study: New Zealand White Rabbits
4. Explain the procedure producing pain and/or distress: Intravenous dosing with one of 3 bioactive compounds through a vascular access port. The challenge procedure itself is not painful but resultant effects were expected to be immediate and severe (with possible resultant death). This work was conducted to determine the threat potential of a naturally occurring compound.
5. Provide scientific justification why pain and/or distress could not be relieved. State methods or means used to determine that pain and/or distress relief would interfere with test results.

Anesthetics, analgesics, and sedatives could not be provided because it had the potential to mask or potentiate the effects of the administered compound and confound results. There are no known characterized, surrogate markers or in vitro methods to predict mortality and development of clinical pathology. Experienced staff veterinarians and animal technicians were on site to monitor the study conduct and any animal welfare issues. Pain-relieving drugs were not used, on the basis that death is rapid following the onset of symptoms, and that the use of pain medications could mask the clinical appearance, affecting the experimental data. These data are critical to human safety in the event of human exposure.

6. N/A

Column E Explanation Form

1. Registration Number: 31-R-0021
2. Number of animals used in this study: 114

3. Species (common name) of animals used in this study: New Zealand White Rabbits
4. Explain the procedure producing pain and/or distress: Aerosol challenge with bacterial spores. The challenge was performed using a muzzle-only exposure chamber. The challenge procedure itself is not painful but resultant bacterial infection may have caused pain and/or distress. This work was conducted to evaluate the effectiveness of monoclonal antibodies, antibiotic treatment and/or vaccination (proprietary).
5. Provide scientific justification why pain and/or distress could not be relieved. State methods or means used to determine that pain and/or distress relief would interfere with test results.

Anesthetics, analgesics, and sedatives could not be provided because it had the potential to mask or potentiate the effects of infection and confound results. There are no known characterized, surrogate markers to predict mortality. Experienced staff veterinarians and animal technicians were on site to monitor the study conduct and any animal welfare issues. Pain-relieving drugs were not used, on the basis that death is rapid following the onset of symptoms, and that the use of pain medications could mask the clinical appearance, affecting the experimental data. Animals exhibiting clinical signs or those which are found to be moribund were euthanized to alleviate pain and distress. These data are critical to human safety in the event of human exposure.

6. What, if any, federal regulations require this procedure? Cite the agency, the Code of Federal Regulations (CFR) title number and the specific section number:

Agency: FDA

CFR: As appropriate, study conducted under Title 21, Food and Drugs, specifically, 21CFR.314.610, approval based on evidence of effectiveness from studies in animals (under subpart I--approval of new drugs when human efficacy studies are not ethical or feasible), and 21CFR601.91, approval based on evidence of effectiveness from studies in animals (under subpart H--approval of biological products when human efficacy studies are not ethical or feasible).

Column E Explanation Form

1. Registration Number: 31-R-0021
2. Number of animals used in this study: 7
3. Species (common name) of animals used in this study: New Zealand White Rabbits
4. Explain the procedure producing pain and/or distress: Aerosol challenge with bacterial spores. The challenge was performed using a muzzle-only exposure chamber. The challenge procedure itself is not painful but resultant bacterial infection may have caused pain and/or distress. This work was conducted to evaluate the disease process in rabbits and was intended to provide data leading to utilization of the rabbit model in therapeutic efficacy studies.
5. Provide scientific justification why pain and/or distress could not be relieved. State methods or means used to determine that pain and/or distress relief would interfere with test results.

Anesthetics, analgesics, and sedatives could not be provided because it had the potential to mask or potentiate the effects of infection and confound results. There are no known characterized, surrogate markers to predict mortality. Experienced staff veterinarians and animal technicians were on site to monitor the study conduct and any animal welfare issues. Pain-relieving drugs were not used, on the basis that death is rapid following the onset of symptoms, and that the use of pain medications could mask the clinical appearance, affecting the experimental data. Animals exhibiting clinical signs or those which are found to be moribund were euthanized to alleviate pain and distress. These data are critical to human safety in the event of human exposure.

6. What, if any, federal regulations require this procedure? Cite the agency, the Code of Federal Regulations (CFR) title number and the specific section number:

This work was conducted to validate a model and develop data necessary for definitive studies [required by the federal government under 21CFR.314.610 - subpart I -approval of new drugs when human efficacy studies are not ethical or feasible, and/or 21CFR601.91 - subpart H -approval of biological products when human efficacy studies are not ethical or feasible].

Column E Explanation Form

1. Registration Number: 31-R-0021
2. Number of animals used in this study: 12
3. Species (common name) of animals used in this study: New Zealand White Rabbits
4. Explain the procedure producing pain and/or distress: Aerosol challenge with bacterial spores. The challenge was performed using a muzzle-only exposure chamber. The challenge procedure itself is not painful but resultant bacterial infection may have caused pain and/or distress.
5. Provide scientific justification why pain and/or distress could not be relieved. State methods or means used to determine that pain and/or distress relief would interfere with test results.

Anesthetics, analgesics, and sedatives could not be provided because it had the potential to mask or potentiate the effects of infection and confound results. There are no known characterized, surrogate markers to predict mortality. Experienced staff veterinarians and animal technicians were on site to monitor the study conduct and any animal welfare issues. Pain-relieving drugs were not used, on the basis that death is rapid following the onset of symptoms, and that the use of pain medications could mask the clinical appearance, affecting the experimental data. Animals exhibiting clinical signs or those which are found to be moribund were euthanized to alleviate pain and distress. These data are critical to human safety in the event of human exposure.

6. What, if any, federal regulations require this procedure? Cite the agency, the Code of Federal Regulations (CFR) title number and the specific section number:

This work was conducted to validate a model and develop data necessary for definitive studies [required by the federal government under 21CFR.314.610 - subpart I -approval of new drugs when human efficacy studies are not ethical or feasible, and/or 21CFR601.91 - subpart H -approval of biological products when human efficacy studies are not ethical or feasible].

Column E Explanation Form

1. Registration Number: 31-R-0021
2. Number of animals used in this study: 56
3. Species (common name) of animals used in this study: New Zealand White Rabbits
4. Explain the procedure producing pain and/or distress: Intramuscular injection. The dosing procedure involved an injection with bacterial spores which did not cause more than momentary pain or distress. The resultant bacterial infection may have caused pain and/or distress. This work was conducted to evaluate the effectiveness of monoclonal antibodies, antibiotic treatment and/or vaccination (proprietary).

5. Provide scientific justification why pain and/or distress could not be relieved. State methods or means used to determine that pain and/or distress relief would interfere with test results.

Anesthetics, analgesics and sedatives may potentiate the effects of infection and could confound results. There are no known characterized, surrogate markers to predict mortality. Experienced staff veterinarians and animal technicians were on site to monitor the study conduct and any animal welfare issues. Pain-relieving drugs were not used, on the basis that death is rapid following the onset of symptoms, and that the use of pain medications could mask the clinical appearance, affecting the experimental data. Animals exhibiting clinical signs or those which were moribund were euthanized to alleviate pain and distress. These data are critical to human safety in the event of human exposure.

6. What, if any, federal regulations require this procedure? Cite the agency, the Code of Federal Regulations (CFR) title number and the specific section number:

This work was conducted to validate a model and develop data necessary for definitive studies [required by the federal government under 21CFR.314.610 - subpart I -approval of new drugs when human efficacy studies are not ethical or feasible, and/or 21CFR601.91 - subpart H -approval of biological products when human efficacy studies are not ethical or feasible].

Column E Explanation Form

1. Registration Number: 31-R-0021

2. Number of animals used in this study: 129

3. Species (common name) of animals used in this study: New Zealand White Rabbits

4. Explain the procedure producing pain and/or distress: Aerosol challenge with bacterial spores. The challenge was performed using a muzzle-only exposure chamber. The challenge procedure itself is not painful but resultant bacterial infection may have caused pain and/or distress. This work was conducted to evaluate the effectiveness of monoclonal antibodies, antibiotic treatment and/or vaccination (proprietary).

5. Provide scientific justification why pain and/or distress could not be relieved. State methods or means used to determine that pain and/or distress relief would interfere with test results.

Anesthetics, analgesics, and sedatives could not be provided because it had the potential to mask or potentiate the effects of infection and confound results. There are no known characterized, surrogate markers to predict mortality. Experienced staff veterinarians and animal technicians were on site to monitor the study conduct and any animal welfare issues. Pain-relieving drugs were not used, on the basis that death is rapid following the onset of symptoms, and that the use of pain medications could mask the clinical appearance, affecting the experimental data. Animals exhibiting clinical signs or those which are found to be moribund were euthanized to alleviate pain and distress. These data are critical to human safety in the event of human exposure.

6. What, if any, federal regulations require this procedure? Cite the agency, the Code of Federal Regulations (CFR) title number and the specific section number:

This work was conducted to validate a model and develop data necessary for definitive studies [required by the federal government under 21CFR.314.610 - subpart I -approval of new drugs when human efficacy studies are not ethical or feasible, and/or 21CFR601.91 - subpart H -approval of biological products when human efficacy studies are not ethical or feasible].

Column E Explanation Form

1. Registration Number: 31-R-0021

2. Number of animals used in this study: 18
3. Species (common name) of animals used in this study: *Cynomolgus macaques*
4. Explain the procedure producing pain and/or distress: Intravenous challenge with a systemic virus to test the protective efficacy of a proprietary vaccine candidate. The challenge was performed under Telazol® anesthesia. The challenge procedure itself is not painful but resultant viral infection may have caused pain and/or distress. This work was conducted to evaluate the effectiveness of vaccination (proprietary).
5. Provide scientific justification why pain and/or distress could not be relieved. State methods or means used to determine that pain and/or distress relief would interfere with test results.

Anesthetics, analgesics, and sedatives could not be provided because it had the potential to mask or potentiate the effects of infection and confound results. There are no known characterized, surrogate markers to predict mortality. Experienced staff veterinarians and animal technicians were on site to monitor the study conduct and any animal welfare issues. Pain-relieving drugs were not used, on the basis that the use of pain medications could mask the clinical appearance, affecting the experimental data. Animals exhibiting clinical signs or those which are found to be moribund were euthanized to alleviate pain and distress. These data are critical to human safety in the event of human exposure.

6. What, if any, federal regulations require this procedure? Cite the agency, the Code of Federal Regulations (CFR) title number and the specific section number:

Agency: FDA

CFR: As appropriate, study conducted under Title 21, Food and Drugs, specifically, 21CFR.314.610, approval based on evidence of effectiveness from studies in animals (under subpart I--approval of new drugs when human efficacy studies are not ethical or feasible), and 21CFR601.91, approval based on evidence of effectiveness from studies in animals (under subpart H--approval of biological products when human efficacy studies are not ethical or feasible).

Column E Explanation Form

1. Registration Number: 31-R-0021
2. Number of animals used in this study: 13
3. Species (common name) of animals used in this study: *Cynomolgus macaques*
4. Explain the procedure producing pain and/or distress: Intravenous challenge with a systemic virus to characterize the optimal dose of the current stock of virus. The challenge was performed under Telazol® anesthesia. The challenge procedure itself is not painful but resultant viral infection may have caused pain and/or distress.
5. Provide scientific justification why pain and/or distress could not be relieved. State methods or means used to determine that pain and/or distress relief would interfere with test results.

Anesthetics, analgesics, and sedatives could not be provided because it had the potential to mask or potentiate the effects of infection and confound results. There are no known characterized, surrogate markers to predict mortality. Experienced staff veterinarians and animal technicians were on site to monitor the study conduct and any animal welfare issues. Pain-relieving drugs were not used, on the basis that the use of pain medications could mask the clinical appearance, affecting the experimental data. Animals exhibiting clinical signs or those which are found to be moribund were euthanized to alleviate pain and distress. These data are critical to human safety in the event of human exposure.

6. What, if any, federal regulations require this procedure? Cite the agency, the Code of Federal Regulations (CFR) title number and the specific section number:

This work was conducted to validate a model and develop data necessary for definitive studies [required by the federal government under 21CFR.314.610 - subpart I -approval of new drugs when human efficacy studies are not ethical or feasible, and/or 21CFR601.91 - subpart H -approval of biological products when human efficacy studies are not ethical or feasible].

Column E Explanation Form

1. Registration Number: 31-R-0021
2. Number of animals used in this study: 9
3. Species (common name) of animals used in this study: Cynomolgus macaques
4. Explain the procedure producing pain and/or distress: Aerosol challenge with infectious bacteria. The challenge was performed under Telazol® anesthesia using a head-only exposure chamber. The challenge procedure itself is not painful but resultant bacterial infection may have caused pain and/or distress. This work was conducted to evaluate the effectiveness of a therapeutic treatment (proprietary).
5. Provide scientific justification why pain and/or distress could not be relieved. State methods or means used to determine that pain and/or distress relief would interfere with test results.

Anesthetics, analgesics, and sedatives could not be provided because it had the potential to mask or potentiate the effects of infection and confound results. There are no known characterized, surrogate markers to predict mortality. Experienced staff veterinarians and animal technicians were on site to monitor the study conduct and any animal welfare issues. Pain-relieving drugs were not used, on the basis that death is rapid following the onset of symptoms, and that the use of pain medications could mask the clinical appearance, affecting the experimental data. Animals exhibiting clinical signs or those which are found to be moribund were euthanized to alleviate pain and distress. These data are critical to human safety in the event of human exposure.

6. What, if any, federal regulations require this procedure? Cite the agency, the Code of Federal Regulations (CFR) title number and the specific section number:

This work was conducted to validate a model and develop data necessary for definitive studies [required by the federal government under 21CFR.314.610 - subpart I -approval of new drugs when human efficacy studies are not ethical or feasible, and/or 21CFR601.91 - subpart H -approval of biological products when human efficacy studies are not ethical or feasible].

Column E Explanation Form

1. Registration Number: 31-R-0021
2. Number of animals used in this study: 20
3. Species (common name) of animals used in this study: Cynomolgus macaques
4. Explain the procedure producing pain and/or distress: Aerosol challenge with bacterial spores. The challenge was performed under Telazol® anesthesia using a head-only exposure chamber. The challenge procedure itself is not painful but resultant bacterial infection may have caused pain and/or distress. This work was conducted to evaluate the effectiveness of vaccination (proprietary).

5. Provide scientific justification why pain and/or distress could not be relieved. State methods or means used to determine that pain and/or distress relief would interfere with test results.

Anesthetics, analgesics, and sedatives could not be provided because it had the potential to mask or potentiate the effects of infection and confound results. There are no known characterized, surrogate markers to predict mortality. Experienced staff veterinarians and animal technicians were on site to monitor the study conduct and any animal welfare issues. Pain-relieving drugs were not used, on the basis that death is rapid following the onset of symptoms, and that the use of pain medications could mask the clinical appearance, affecting the experimental data. Animals exhibiting clinical signs or those which are found to be moribund were euthanized to alleviate pain and distress. These data are critical to human safety in the event of human exposure.

6. What, if any, federal regulations require this procedure? Cite the agency, the Code of Federal Regulations (CFR) title number and the specific section number:

This work was conducted to validate a model and develop data necessary for definitive studies [required by the federal government under 21CFR.314.610 - subpart I -approval of new drugs when human efficacy studies are not ethical or feasible, and/or 21CFR601.91 - subpart H -approval of biological products when human efficacy studies are not ethical or feasible].

Column E Explanation Form

1. Registration Number: 31-R-0021
2. Number of animals used in this study: 5
3. Species (common name) of animals used in this study: Rhesus macaques
4. Explain the procedure producing pain and/or distress: Aerosol challenge with bacterial spores. The challenge was performed under Telazol® anesthesia using a head-only exposure chamber. The challenge procedure itself is not painful but resultant bacterial infection may have caused pain and/or distress. This work was conducted to determine early markers of exposure. This work is important to establish procedures at the CDC for measuring markers of exposure.
5. Provide scientific justification why pain and/or distress could not be relieved. State methods or means used to determine that pain and/or distress relief would interfere with test results.

Anesthetics, analgesics, and sedatives could not be provided because it had the potential to mask or potentiate the effects of infection and confound results. Experienced staff veterinarians and animal technicians were on site to monitor the study conduct and any animal welfare issues. Pain-relieving drugs were not used, on the basis that death is rapid following the onset of symptoms, and that the use of pain medications could mask the clinical appearance, affecting the experimental data. Animals exhibiting clinical signs or those which are found to be moribund were euthanized to alleviate pain and distress. These data are critical to human safety in the event of human exposure.

6. What, if any, federal regulations require this procedure? Cite the agency, the Code of Federal Regulations (CFR) title number and the specific section number:

The Division of Laboratory Sciences (DLS), National Center for Environmental Health (NCEH), Centers for Disease Control and Prevention (CDC), is developing methods to rapidly identify toxic substances to which human beings have been exposed. Exposures may be due to chemical or biological emergencies or to acts of terrorism. The purpose of this task order is to help understand the timing of the appearance of a marker in the serum of infected animals and to determine the earliest time point post infection at which it can be detected. These studies will be used to validate an analysis method for early detection of exposure in humans

Column E Explanation Form

1. Registration Number: 31-R-0021
2. Number of animals used in this study: 19
3. Species (common name) of animals used in this study: Rhesus macaques
4. Explain the procedure producing pain and/or distress: Aerosol challenge with bacterial spores. The challenge was performed under Telazol® anesthesia using a head-only exposure chamber. The challenge procedure itself is not painful but resultant bacterial infection may have caused pain and/or distress. This work was conducted to evaluate the protective efficacy of the licensed vaccine using an alternate immunization regimen and aerosol challenge over an extended time interval.
5. Provide scientific justification why pain and/or distress could not be relieved. State methods or means used to determine that pain and/or distress relief would interfere with test results.

Anesthetics, analgesics, and sedatives could not be provided because it had the potential to mask or potentiate the effects of infection and confound results. There are no known characterized, surrogate markers to predict mortality and that is part of the objective of this study. Experienced staff veterinarians and animal technicians were on site to monitor the study conduct and any animal welfare issues. Pain-relieving drugs were not used, on the basis that death is rapid following the onset of symptoms, and that the use of pain medications could mask the clinical appearance, affecting the experimental data. Animals exhibiting clinical signs or those which are found to be moribund were euthanized to alleviate pain and distress. These data are critical to human safety in the event of human exposure.

6. What, if any, federal regulations require this procedure? Cite the agency, the Code of Federal Regulations (CFR) title number and the specific section number:

Agency: FDA

CFR: As appropriate, study conducted under Title 21, Food and Drugs, specifically, 21CFR.314.610, approval based on evidence of effectiveness from studies in animals (under subpart I--approval of new drugs when human efficacy studies are not ethical or feasible), and 21CFR601.91, approval based on evidence of effectiveness from studies in animals (under subpart H--approval of biological products when human efficacy studies are not ethical or feasible).

Column E Explanation Form

1. Registration Number: 31-R-0021
2. Number of animals used in this study: 8
3. Species (common name) of animals used in this study: Rhesus macaques
4. Explain the procedure producing pain and/or distress: Aerosol challenge with bacterial spores. The challenge was performed under Telazol® anesthesia using a head-only exposure chamber. The challenge procedure itself is not painful but resultant bacterial infection may have caused pain and/or distress. This work was conducted to evaluate the effectiveness of monoclonal antibodies, antibiotic treatment and/or vaccination (proprietary).
5. Provide scientific justification why pain and/or distress could not be relieved. State methods or means used to determine that pain and/or distress relief would interfere with test results.

Anesthetics, analgesics, and sedatives could not be provided because it had the potential to mask or potentiate the effects of infection and confound results. There are no known characterized, surrogate markers to predict mortality. Experienced staff veterinarians and animal technicians were on site to monitor the study conduct and any animal welfare issues. Pain-relieving drugs were not used, on the basis that death is rapid following the onset of symptoms, and that the use of pain medications could mask the clinical appearance, affecting the experimental data. Animals exhibiting clinical signs or those which are found to be moribund were euthanized to alleviate pain and distress. These data are critical to human safety in the event of human exposure.

6. What, if any, federal regulations require this procedure? Cite the agency, the Code of Federal Regulations (CFR) title number and the specific section number:

This work was conducted to validate a model and develop data necessary for definitive studies [required by the federal government under 21CFR.314.610 - subpart I -approval of new drugs when human efficacy studies are not ethical or feasible, and/or 21CFR601.91 - subpart H -approval of biological products when human efficacy studies are not ethical or feasible].